| Substitute Form PTO-1449 (Modified)   | U.S. Department of Commerce<br>Patent and Trademark Office |                              | Application No. 10/031,005 |  |
|---|--|------------------------------|----------------------------|--|
| Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR §1.98(b)) |  | Applicant Gary L. Nelsestuen |                            |  |
|   |  | Filing Date October 29, 2001 | Group Art Unit<br>1656     |  |

|                     | U.S. Patent Documents |                    |                     |                 |       |          |                            |
|---------------------|-----------------------|--------------------|---------------------|-----------------|-------|----------|----------------------------|
| Examiner<br>Initial | Desig.<br>ID          | Document<br>Number | Publication<br>Date | Patentee        | Class | Subclass | Filing Date If Appropriate |
| B                   | AA                    | 6,806,063          | 10/19/2004          | Pedersen et al. | ~     |          |                            |
| 5                   | AB                    |                    |                     |                 |       |          |                            |

| Foreign Patent Documents or Published Foreign Patent Applications |        |             |             |               |       |             |     |         |
|---|--------|-------------|-------------|---------------|-------|-------------|-----|---------|
| Examiner  | Desig. | Document    | Publication | Country or    |       | <del></del> |     | slation |
| Initial   | ID     | Number      | Date        | Patent Office | Class | Subclass    | Yes | No      |
| 43  | AC     | WO 01/58935 | 8/16/2001   | WIPO          |       |             |     |         |
|   | AD     |             |             |               |       |             |     |         |

|          | Other D | ocuments (include Author, Title, Date, and Place of Publication)   |
|----------|---------|--|
| Examiner | Desig.  |  |
| Initial  | ID      | Document   |
| 15       | AE      | GenBank® Accession No. M13132 (2/13/1996)  |
| #5       | AF      | "Docking of Tissue Factor and Factor VIIa Initiates Blood Coagulation," at http://www.sdsc.edu.IOTW/week46.96/ (1996)  |
| 85       | AG      | Dickinson and Ruf, "Active Site Modification of Factor VIIa Affects Interactions of the Protease Domain with Tissue Factor," J. Biol. Chem., 1997, 272(32):19875-19879   |
| #        | AH      | Jurlander et al., "Recombinant Activated Factor VII (rFVIIa): Characterization, Manufacturing, and Clinical Development," Semin. Thromb. Hemos., 2001, 27(4):373-383   |
| 45       | AI      | Leff, "Genetically Stripped-Down Factor VIII Corrects Bleeding Disorder in Hemophiliac Mice," BioWorld Today, 1997, 8(209):1,6   |
| H        | AJ      | Martinez et al., "Underdecarboxlyation of Vitamin K-Dependent Proteins: Occasionally Severe, Possibly Universal," Proceedings of the 49th ASMS Conference on Mass Spectrometry and Allied Topics, May 27-31, 2001, Chicago, Illinois, 2 pgs. |
| 115      | AK      | Nelsestuen et al., "Elevated Function of Blood Clotting Factor VIIa Mutants That Have Enhanced Affinity for Membranes," J. Biol. Chem., 2001, 276(43):39825-39831  |
| th       | AL      | Ruf et al., "Importance of Factor VIIa Gla-Domain Residue Arg-36 for Recognition of the Macromolecular Substrate Factor X Gla-Domain," Biochemistry, 1999, 38:1957-1966  |
| B        | AM      | Sakai et al., "The γ-Carboxyglutamic Acid Domain of Human Factor VIIA is Essential for Its Interaction with Cell Surface Tissue Factor," J. Biol. Chem., 1990, 265(4):1890-1894  |
| 45       | AN      | Thim et al., "Amino Acid Sequence and Posttranslational Modification of Human Factor VIIa from Plasma and Transfected Baby Hamster Kidney Cells," Biochemistry, 1988, 27:7785-7793   |
|          | AO      |  |

| Examiner Signature   | Date Considered   |
|--|---|
| Hally: S/  | 8-9-06  |
| EXAMINER: Initials citation considered. Draw line through citati | on if not in conformance and not considered. Include copy of this form with |
| next communication to applicant.                                 |   |

|   | bstitute Form PTO-1449 |
|---|------------------------|
|   | edified)               |
| - | Information            |
|   | ❤ \information         |

U.S. Department of Commerce Patent and Trademark Office

Attorney's Docket No. 09531-016002

Application No. 10/031,005

formation Disclosure Statement by Applicant (Use several sheets if necessary) Applicant
Gary L. Nelsestuen

Filing Date

Group Art Unit

October 29, 2001

1656

| U.S. Patent Documents |              |                    |                     |                   |       |          |                            |
|-----------------------|--------------|--------------------|---------------------|-------------------|-------|----------|----------------------------|
| Examiner<br>Initial   | Desig.<br>ID | Document<br>Number | Publication<br>Date | Patentee          | Class | Subclass | Filing Date If Appropriate |
| 1:15                  | AA           | 4,784,950          | 11/15/1988          | Hagen et al.      | 1     |          |                            |
| 1                     | AB           | 4,904,584          | 2/27/1990           | Shaw              |       | _        |                            |
|                       | AC           | 5,041,376          | 8/20/1991           | Gething et al.    |       |          |                            |
|                       | AD           | 5,180,583          | 1/19/1993           | Hedner            | _     | -        | •                          |
|                       | AE           | 5,225,537          | 7/6/1993            | Foster            | _     |          |                            |
|                       | AF           | 5,460,950          | 10/24/1995          | Barr et al.       | _     |          |                            |
|                       | AG           | 5,648,254          | 7/15/1997           | Mulvihill et al.  | _     | _        |                            |
|                       | AH           | 5,891,843          | 4/6/1999            | Turecek et al.    |       |          |                            |
|                       | AI           | 5,965,425          | 10/12/1999          | Barr et al.       | _     |          |                            |
|                       | AJ           | 5,986,079          | 11/16/1999          | Barr et al.       | _     |          | ·                          |
|                       | AK           | 6,013,620          | 1/11/2000           | Turecek et al.    |       |          |                            |
|                       | AL           | 6,100,061          | 8/8/2000            | Reiter et al.     | _     | _        |                            |
|                       | AM           | 6,423,826          | 7/23/2002           | Nelsestuen et al. |       |          |                            |
|                       | AN           | 6,475,725          | 11/5/2002           | Reiter et al.     |       | (        |                            |
|                       | AO           | 6,693,075          | 2/17/2004           | Nelsestuen        | _     | _        |                            |
|                       | AP           | 6,747,003          | 6/8/2004            | Nelsestuen        | _     |          |                            |
|                       | AQ           | 6,762,286          | 7/13/2004           | Nelsestuen        |       | _        |                            |
|                       | AR           | 6,903,069          | 6/7/2005            | Pingel et al.     | _     |          |                            |
|                       | AS           | 2003/0100506       | 11/18/2002          | Nelsestuen        | _     |          |                            |
|                       | AT           | 2003/0100740       | 11/15/2002          | Persson et al.    | _     |          |                            |
|                       | AU           | 2003/0104978       | 9/13/2001           | Persson et al.    | -     |          |                            |
|                       | AV           | 2003/0211094       | 12/30/2002          | Nelsestuen        | -     |          |                            |
| HS                    | AW           | 2003/0211460       | 12/30/2002          | Nelsestuen        | -     |          |                            |

| Foreign Patent Documents or Published Foreign Patent Applications  |        |          |             |            |       |          |             |
|--|--------|----------|-------------|------------|-------|----------|-------------|
| Examiner   | Desig. | Document | Publication | Country or | Class | Subclass | Translation |
| Examiner Signature  Date Considered  9-5-06  |        |          |             |            |       |          |             |
| EXAMINER: Initials citating considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |        |          |             |            |       |          |             |
| Substitute Disclosure Form (PTO-1449)  |        |          |             |            |       |          |             |

Substitute Form PTO-1449 (Modified) U.S. Department of Commerce Patent and Trademark Office Application No. Attomey's Docket No. 09531-016002 10/031,005 Applicant Information Disclosure Statement by Applicant (Use several sheets if necessary) Gary L. Nelsestuen Filing Date **Group Art Unit** October 29, 2001 1656

| ENTATRAGE |     |                |            |                   |   | Yes | No |
|-----------|-----|----------------|------------|-------------------|---|-----|----|
| 145       | AX  | WO 91/11514    | 8/8/1991   | WIPO              |   |     |    |
|           | AY  | WO 92/15686    | 9/17/1992  | WIPO              |   |     |    |
|           | AZ  | WO 94/27631    | 12/8/1994  | WIPO              |   |     |    |
|           | AAA | WO 96/00577    | 1/11/1996  | WIPO              |   |     |    |
|           | ABB | WO 98/32466    | 7/30/1998  | WIPO              |   |     |    |
|           | ACC | WO 98/35026    | 8/13/1998  | WIPO <sub>.</sub> |   |     |    |
|           | ADD | WO 99/03498    | 1/28/1999  | WIPO              |   |     |    |
|           | AEE | WO 99/03887    | 1/28/1999  | WIPO              |   |     |    |
|           | AFF | WO 99/66031    | 12/23/1999 | WIPO              |   |     |    |
|           | AGG | WO 00/26230    | 5/11/2000  | WIPO              |   |     |    |
|           | AHH | WO 00/26354    | 5/11/2000  | WIPO              |   |     |    |
|           | AII | WO 00/28065    | 5/18/2000  | WIPO              |   |     | ,  |
|           | AJJ | WO 00/54787    | 9/21/2000  | WIPO              |   |     |    |
|           | AKK | WO 00/66753    | 11/9/2000  | WIPO              | * |     |    |
|           | ALL | WO 01/83725    | 11/8/2001  | WIPO              |   |     |    |
|           | AMM | WO 02/02764    | 1/10/2002  | WIPO              |   |     |    |
|           | ANN | WO 02/03075    | 1/10/2002  | WIPO              |   |     |    |
|           | AOO | WO 02/077218   | 10/3/2002  | WIPO              |   |     |    |
|           | APP | WO 02/22776    | 3/21/2002  | WIPO              |   |     |    |
|           | AQQ | WO 02/29025    | 4/11/2002  | WIPO              |   |     |    |
|           | ARR | WO 02/38162    | 5/16/2002  | WIPO              |   |     |    |
|           | ASS | WO 03/027147   | 4/3/2003   | WIPO              |   |     |    |
|           | ATT | WO 03/037932   | 5/8/2003   | WIPO              |   |     |    |
|           | AUU | WO 03/055512   | 7/10/2003  | WIPO              |   |     |    |
|           | AVV | WO 03/093465   | 11/13/2003 | WIPO              |   |     |    |
|           | AWW | WO 2004/029091 | 4/8/2004   | WIPO              | 1 |     |    |
|           | AXX | WO 2004/083361 | 9/30/2004  | WIPO              |   |     |    |
|           | AYY | EP 0 370 205   | 5/30/1990  | EPO               |   |     |    |
| 145       | AZZ | EP 0 512 011   | 11/11/1992 | EPO               |   |     |    |

| Examiner Signature  | Date Considered 9-5-0 W |  |  |  |  |
|---|-------------------------|--|--|--|--|
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with |                         |  |  |  |  |
| next communication to applicant. (  |                         |  |  |  |  |

Substitute Form PTO-1449
U.S. Department of Commerce Patent and Trademark Office

Attorney's Docket No. 09531-016002

Application No. 10/031,005

Applicant Gary L. Nelsestuen

Filing Date October 29, 2001

Group Art Unit 1656

|                  | Other Do     | ocuments (include Author, Title, Date, and Place of Publication)   |
|------------------|--------------|--|
| Examiner Initial | Desig.<br>ID | Document   |
| ft5              | AAAA         | Bharadwaj et al., "Factor VII central. A novel mutation in the catalytic domain that reduces tissue factor binding, impairs activation by factor Xa, and abolishes amidolytic and coagulant activity," J. Biol. Chem., 1996, 271:30685-30691                                 |
| ·                | ABBB         | Bjoern et al., "Human plasma and recombinant factor VII. Characterization of O-glycosylations at serine residues 52 and 60 and effects of site-directed mutagenesis of serine 52 to alanine," J. Biol. Chem. 1991, 266(17):11051-11057                                       |
|                  | ACCC         | Chang et al., "Engineered recombinant factor VII Q217 variants with altered inhibitor specificities," Biochemistry 1999, 38:10940-10948  |
|                  | ADDD         | Chang et al., "Replacing the first epidermal growth factor-like domain of factor IX with that of factor VII enhances activity in vitro and in canine hemophilia B," J. Clin. Invest. 1997, 100(4), 886-892   |
|                  | AEEE         | Cheung et al., "Localization of a metal-dependent epitope to the amino terminal residues 33-40 of human factor IX," Thrombosis Res. 1995, 80(5): 419-427   |
|                  | AFFF         | EMBL Accession No. AF465270 (2/2/2003)   |
|                  | AGGG         | UNIPROT Accession No. P22457 (8/1/1991)  |
|                  | АННН         | Dickinson et al., "Influence of cofactor binding and active site occupancy on the conformation of the macromolecular substrate exosite of factor VIIa," J. Mol. Biol. 1998, 277:959-971  |
|                  | AIII         | Dickinson et al., "Identification of surface residues mediating tissue factor binding and catalytic function of the serine protease factor VIIa," Proc. Natl. Acad. Sci. 1996, 93:14379-14384  |
|                  | AJJJ         | Hedner et al., "NovoSeven as a universal haemostatic agent," Blood Coagulation & Fibrinolysis 2000:11:107-111  |
|                  | AKKK         | Higashi et al., "Molecular mechanism of tissue factor-mediated acceleration of factor VIIa activity," J. Biol. Chem. 1996, 271(43):26569-26574   |
|                  | ALLL         | Huang et al., "Substrate Recognition by Tissue Factor-Factor VIIa. Evidence for interaction of residues Lys165 and Lys166 of tissue factor with the 4-carboxyglutamate-rich domain of factor X"  J. Biol. Chem. 1996, 271(36):21752-21757                                    |
|                  | AMMM         | Iino et al., "Functional consequences of mutations in Ser-52 and Ser-60 in human blood coagulation factor VII," Archives of Biochemistry and Biophysics 1998, 352(2):182-192   |
|                  | ANNN         | Iakhiaev et al., "The Role of Catalytic Cleft & Exosite Residues of Factor VIIa for Complex Formation with Tissue Factor Pathway Inhibitor" Thromobsis & Haemostasis 2001, 85:458-463  |
|                  | A000         | Jin et al., "Factor VIIa's first epidermal growth factor-like domain's role in catalytic activity,"<br>Biochemistry 1999, 38:1185-1192   |
|                  | APPP         | Jin et al., "Four loops of the catalytic domain of factor viia mediate the effect of the first EGF-like domain substitution on factor viia catalytic activity," J. Mol. Biol. 2001, 307:1503-1517  |
|                  | AQQQ         | Kelly et al., "Ca <sup>2+</sup> binding to the first epidermal growth factor module of coagulation factor VIIa is important for cofactor interaction and proteolytic function," J. Biol. Chem. 1997, 272(28):17467-17472   |
| 15               | ARRR         | Kemball-Cook et al., "Coagulation Factor VII Gln <sup>100</sup> Arg. Amino acid substitution at the epidermal growth factor 2-protease domain interface results in severely reduced tissue factor binding and procoagulant function," J. Biol. Chem. 1998, 273(14):8516-8521 |

| Examiner Signature / / //   | Date Considered  |
|---|--|
| Hully of  | 9-5-06   |
| EXAMINER: Initials distion considered. Draw line through citation if no | ot in conformance and not considered. Include copy of this form with |
| next communication to applicant.  |  |
|   | Substitute Disclosure Form (PTO-1449)                                |

|   |   |  |                                    |                            | - |
|---|---|--|------------------------------------|----------------------------|---|
| _ | Substitute Form PTO-1449 (Modified)           | U.S. Department of Commerce<br>Patent and Trademark Office | Attorney's Docket No. 09531-016002 | Application No. 10/031,005 |   |
| • | Information Disclosure Statement by Applicant |  | Applicant Gary L. Nelsestuen       |                            |   |
| J | (Use several sh                               | (Use several sheets if necessary)                          | Filing Date October 29, 2001       | Group Art Unit             |   |

| Fyaminer | Other Documents (include Author, Title, Date, and Place of Publication)  |   |  |  |  |
|----------|--|---|--|--|--|
| LACITION | 1 -00.9.   |   |  |  |  |
| Initial  | ID I   | Document  |  |  |  |
| NS       | ASSS   | Leonard et al., "Activation and Active Site Occupation Alter Conformation in the Region of the First Epidermal Growth Factor-like Domain of Human Factor VII," J. Biol. Chem. 2000, 275(45):34894-34900 |  |  |  |
|          | ATTT   | Mayer, "Ultra-early hemostatic therapy for intracerebral hemorrhage," Stroke 2003, 34:224-229   |  |  |  |
|          | AUUU   | Neuenschwander et al., "Alteration of the substrate and inhibitor specificities of blood coagulation," Biochemistry 1995, 34:8701-8707  |  |  |  |
|          | AVVV Persson et al., "Ca <sup>2+</sup> binding to the first epidermal growth factor-like domain of factor VIIa increases amidolytic activity and tissue factor affinity," J. Biol. Chem. 1997, 272(32):19919-19924   |   |  |  |  |
|          | AWWW Persson, "Characterization of the interaction between the light chain of factor VIIa and tissue factor," FEBS Letters 1997, 413:359-363  AXXX Petersen et al., "Binding of Zn <sup>2+</sup> to a Ca <sup>2+</sup> loop allosterically attenuates the activity of factor VI and reduces its affinity for tissue factor," Protein Science 2000, 9:859-866 |   |  |  |  |
|          |  |   |  |  |  |
|          | AYYY   | Petrovan et al., "Role of residue Phe <sup>225</sup> in the cofactor-mediated, allosteric regulation of the serine protease coagulation factor VIIa," Biochemistry 2000, 39:14457-14463                 |  |  |  |
|          | AZZZ   | Petrovan et al., "Residue Met <sup>156</sup> contributes to the labile enzyme conformation of coagulation factor VIIa," J. Biol. Chem. 2001, 276(9):6616-6620   |  |  |  |
|          | AAAAA  | Shobe et al., "Regulation of the catalytic function of coagulation factor VIIa by a conformational linkage of surface residue Glu 154 to the active site," Biochemistry 1999, 38:2745-2751              |  |  |  |
|          | ABBBB  | Shobe et al., "Macromolecular substrate affinity for the tissue factor-factor VIIa complex is independent of scissile bond docking," J. Biol. Chem. 1999, 274(34):24171-24175                           |  |  |  |
|          | ACCCC  | Sridhara et al., "Activation of a recombinant human factor VII structural analogue alters its affinity of binding to tissue factor," Amer. J. Hemotology 1996, 53:66-71                                 |  |  |  |
| HS       | ADDDD  | Zhang et al., "Structure of extracellular tissue factor complexed with factor VIIa inhibited with a BPTI mutant," J. Mol. Biol. 1999, 285(5):2089-2104  |  |  |  |

| Examiner Signature  | Date Considered |  |
|---|-----------------|--|
| Large Day   | 9-5-06          |  |
| EXAMINER: Initials distribute considered. Draw line through distribution if not in conformance and not considered. Include copy of this form with |                 |  |